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July 15, 2004

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Re: U.S. Patent Application No.: 09/995519
For: *Methods for Modulating T Cell Unresponsiveness*
Inventors: Boussiotis, V.A., et al.
Filed: November 28, 2001
Our Ref. No.: RPI-011CPCN

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Information Disclosure Statement;
2. PTO Form 1449; and
3. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

I hereby certify that this correspondence is deposited with the United States Postal Service as first class mail in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450:

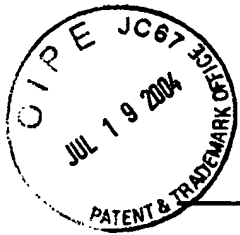
July 15, 2004

Date

DeAnn F. Smith, Esq., Reg. No. 36,683

Respectfully submitted,
LAHIVE & COCKFIELD, LLP

DeAnn F. Smith, Esq.
Registration No. 36,683
Attorney for Applicants



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Boussiotis, V.A., *et al.*

Serial No.: 09/995519

Filed: November 28, 2001

For: *Methods for Modulating T Cell Unresponsiveness*

Attorney Docket No.: RPI-011CPCN

Group Art Unit: 1644

Examiner: Phillip Gambel

MS Amendment
Commissioner for Patents
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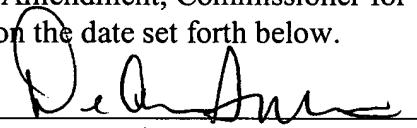
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July 15, 2004

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By:


DeAnn F. Smith, Esq.
Registration No. 36,683
Attorney for Applicants

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

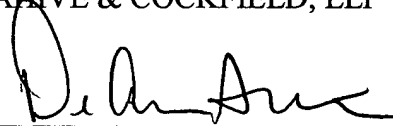
Applicants and their Attorney are aware of the following patents, publications or other information, which are cited on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration.

The present application is a Continuation Application of U.S. Serial No. 08/457483, filed June 1, 1995 (Atty. Docket No. RPI-011CP). All references listed on the enclosed PTO Form 1449 have been previously cited by or submitted to the Office in the prior application, and, in accordance with 37 CFR §1.98(d), copies of these references are not enclosed herewith, but will be provided upon request.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(3), no additional costs are believed to be due in connection with the filing of this disclosure. If, however, a first Office Action on the merits issues in this application bearing a mailing date prior to the date of this Information Disclosure Statement, please charge the appropriate fee as required under 37 CFR §1.17(p) to our Deposit Order Account No. 12-0080.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP

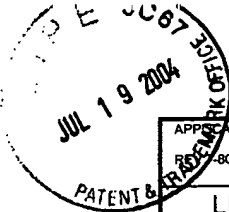


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Date: July 15, 2004

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| APPLICANT FACSIMILE OF FORM PTO-1449 REV. 1-90 | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTY DOCKET NO RPI-011CPCN | SERIAL NO. 09/995519 |
| LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary) | | APPLICANT Boussiotis, V.A., et al. | |
| | | FILING DATE November 28, 2001 | GROUP 1644 |

U.S. PATENT DOCUMENTS

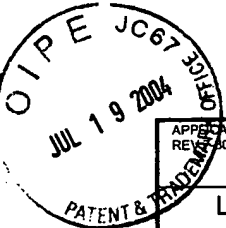
| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|---------------------|----|-----------------|---------|----------------|-------|----------|-------------------------------|
| | AA | 5,116,964 | 5/26/92 | Capon et al | 536 | 27 | |
| | AB | 5,434,131 | 7/18/95 | Linsley et al. | 514 | 2 | |

FOREIGN PATENT DOCUMENTS

| | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION | |
|--|----|-----------------|---------|---------|-------|----------|-------------|----|
| | | | | | | | YES | NO |
| | AC | WO 90/05541 | 5/31/90 | PCT | | | | |
| | AD | WO 91/11194 | 8/8/91 | PCT | | | | |
| | AE | WO 92/00092 | 1/9/92 | PCT | | | | |
| | AF | WO 92/15671 | 9/17/92 | PCT | | | | |
| | AG | 0503646 A1 | 12/3/92 | EPO | | | | |
| | AH | WO 93/00431 | 1/7/93 | PCT | | | | |
| | AI | WO 93/06852 | 4/15/93 | PCT | | | | |
| | AJ | WO 93/06866 | 4/15/93 | PCT | | | | |

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

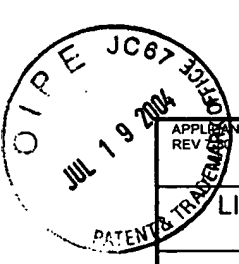
| | | |
|-----------|----|--|
| | AK | Azuma, M., et al., "B70 Antigen is a Second Ligand for CTLA-4 and CD28," <i>Nature</i> , vol. 366, 76-79 (1993); |
| | AL | Bell, G. and Imboden, J., "CD2 and the Regulation of T Cell Anergy," <i>The Journal of Immunology</i> , 2805-2807 (1995); |
| | AM | Beverly, B., et al., "Reversal of in Vitro T Cell Clonal Anergy by IL-2 Stimulation," <i>International Immunology</i> , vol. 4, no. 6, 661-671 (1992); |
| | AN | Bierer, B., et al., "Interaction of CD2 with its Ligand, LFA-3; in Human T Cell Proliferation," <i>The Journal of Immunology</i> , vol. 140, no. 10, 3358-3363 (1988); |
| | AO | Bierer, B., et al., "Synergistic T Cell Activation Via the Physiological Ligands for CD2 and the T Cell Receptor," <i>J. Exp. Med.</i> , vol. 168, 1145-1156 (1988); |
| | AP | Boussiotis, V., et al., "B7 but not Intercellular Adhesion Molecule-1 Costimulation Prevents the Induction of Human Alloantigen-specific Tolerance," <i>J. Exp. Med.</i> , vol. 178, 1753-1763 (1993); |
| | AQ | Boussiotis, V., et al., "CD2 is Involved in Maintenance and Reversal of Human Alloantigen-specific Clonal Anergy," <i>J. Exp. Med.</i> , vol. 180, 1665-1673 (1994); |
| | AR | Boussiotis, V., et al., "Human Alloantigen Specific Clonal Anergy to Lymphoblastoid Cells is Reversed Following Culture with IL-2 or IL-4," <i>Blood</i> , vol. 82, 304A (1993); |
| | AS | Brottier, P., et al., "T Cell Activation Via CD2 [T, gp50] Molecules: Accessory Cells are Required to Trigger T Cell Activation Via CD2-D66 Plus CD2-9.6/T11; Epitopes," <i>The Journal of Immunology</i> , vol. 135, no. 3, 1624-1631 (1985); |
| Examiner | | Date Considered |
| *EXAMINER | | Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |



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| APPLICANT FACSIMILE OF FORM PTO-1449 REVISED 10 | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTY DOCKET NO RPI-011CPCN | SERIAL NO. 09/995519 |
| LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary) | | APPLICANT Boussiotis, V.A., et al. | |
| | | FILING DATE November 28, 2001 | GROUP 1644 |

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|-----------|----|--|
| | BA | Dustin, M., et al., "Anchoring Mechanisms for LFA-3 Cell Adhesion Glycoprotein at Membrane Surface," <i>Nature</i> , vol. 329, 846-848 (1987); |
| | BB | Freedman, A., et al., "B7, a B Cell-Restricted Antigen that Identifies Preactivated B Cells," Division of Tumor Immunology, Dana-Farber Cancer Institute and the Department of Medicine, 3260-3267 (1987); |
| | BC | Freeman, G., et al., "B7, a new Member of the Ig Superfamily with Unique Expression on Activated and Neoplastic B Cells," <i>The Journal of Immunology</i> , vol. 143, no. 8, 2714-2722 (1989); |
| | BD | Freeman, G., et al., "Cloning of B7-2: A CTLA-4 Counter-Receptor that Costimulates Human T Cell Proliferation," <i>Science</i> , vol. 262, 909-911 (1993); |
| | BE | Freeman, G., et al., "Murine B7-2, an Alternative CTLA4 Counter-receptor that Costimulates T Cell Proliferation and Interleukin 2 Production," <i>The Journal of Experimental Medicine</i> , vol. 178, 2185-2192 (1993); |
| | BF | Freeman, G., et al., "Structure, Expression, and T Cell Costimulatory Activity of the Murine Homologue of the Human B Lymphocyte Activation Antigen B7," <i>J. Exp. Med.</i> , vol. 174, 625-631 (1991); |
| | BG | Freeman, G., et al., "Uncovering of Functional Alternative CTLA-4 Counter-Receptor in B7-Deficient Mice," <i>Science</i> , vol. 262, 907-909 (1993); |
| | BH | Gimmi, C., et al., "B-cell Surface Antigen B7 Provides a Costimulatory Signal that Induces T Cells to Proliferate and Secrete Interleukin 2," <i>Proc. Natl. Acad. Sci. USA</i> , vol. 88, 6575-6579 (1991); |
| | BI | Gimmi, C., et al., "Human T-cell Clonal Anergy is Induced by Antigen Presentation in the Absence of B7 Costimulation," <i>Proc. Natl. Acad. Sci. USA</i> , vol. 90, 6586-6590 (1993); |
| | BJ | Harding, F., et al., "CD28-mediated Signaling Co-stimulates Murine T Cells and Prevents Induction of Anergy in T-cell Clones," <i>Nature</i> , vol. 356, 607-609 (1992); |
| | BK | Hathcock, K., et al., "Identification of an Alternative CTLA-4 Ligand Costimulatory for T Cell Activation," <i>Science</i> , vol. 262, 905-907 (1993); |
| | BL | Koyasu, S., et al., "Role of Interaction of CD2 Molecules with Lymphocyte Function-associated Antigen 3 in T-cell Recognition of Nominal Antigen," <i>Proc. Natl. Acad. Sci. USA</i> , vol. 87, 2603-2607 (1990); |
| | BM | Lenschow, D., et al., "Long-Term Survival of Xenogeneic Pancreatic Islet Grafts Induced by CTLA4Ig," <i>Science</i> , vol. 257, 789-791 (1992); |
| | BN | Lin, H., et al., "Long-Term Acceptance of Major Histocompatibility Complex Mismatched Cardiac Allografts Induced by CTLA4Ig Plus Donor-specific Transfusion," <i>J. Exp. Med.</i> , vol. 178, 1801-1806 (1993); |
| | BO | Linsley, P., et al., "Binding of the B Cell Activation Antigen B7 to CD28 Costimulates T Cell Proliferation and Interleukin 2 mRNA Accumulation," <i>J. Exp. Med.</i> , vol. 173, 721-730 (1991); |
| | BP | Linsley, P., et al., "Immunosuppression in Vivo by a Soluble Form of the CTLA-4 T Cell Activation Molecule," <i>Science</i> , vol. 257, 792-795 (1992); |
| | BQ | Meuer, S., et al., "An Alternative Pathway of T-Cell Activation: A Functional Role for the 50 kd T11 Sheep Erythrocyte Receptor Protein," <i>Cell</i> , vol. 36, 897-906 (1984); |
| | BR | Moingeon, P., et al., "CD2-mediated Adhesion Facilitates T Lymphocyte Antigen Recognition Function," <i>Nature</i> , vol. 339, 312-314 (1989); |
| Examiner | | Date Considered |
| *EXAMINER | | Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |



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| APPLICANT FACSIMILE OF FORM PTO-1449 REV 10/97 | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTY DOCKET NO RPI-011CPCN | SERIAL NO. 09/995519 |
| LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary) | | APPLICANT Boussiotis, V.A., et al. | |
| | | FILING DATE November 28, 2001 | GROUP 1644 |

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|-----------|----|--|
| | CA | Pepinsky, R., et al., "The Increased Potency of Cross-linked Lymphocyte Function-associated Antigen-3 (LFA-3) Multimers is a Direct Consequence of Changes in Valency," <i>The Journal of Biological Chemistry</i> , vol. 266, no. 27, 18244-18249 (1991); |
| | CB | Seed, B., "An LFA-3 cDNA Encodes a Phospholipid-linked Membrane Protein Homologous to its Receptor CD2," <i>Nature</i> , vol. 329, 840-842 (1987); |
| | CC | Selvaraj, P., et al., "The T Lymphocyte Glycoprotein CD2 Binds the Cell Surface Ligand LFA-3," <i>Nature</i> , vol. 326, 400-403 (1987); |
| | CD | Tan, P., et al., "Induction of Alloantigen-specific Hyporesponsiveness in Human T Lymphocytes by Blocking Interaction of CD28 with its Natural Ligand B7/BB1," <i>J. Exp. Med.</i> , vol. 177, 165-173 (1993); |
| | CE | Van Gool, S., et al., "The Combination of Anti-B7 Monoclonal Antibody and Cyclosporin A Induces Alloantigen-specific Anergy During a Primary Mixed Lymphocyte Reaction," <i>J. Exp. Med.</i> , vol. 179, 715-720 (1994); |
| | CF | Wallner, B., et al., "Primary Structure of Lymphocyte Function-Associated Antigen 3 (LFA-3) The Ligand of the T Lymphocyte CD2 Glycoprotein," <i>Journal of Experimental Medicine</i> , vol. 166, 923-932 (1987); |
| | CG | Yang, S., et al., "A Common Pathway for T Lymphocyte Activation Involving Both the CD3-Ti Complex and CD2 Sheep Erythrocyte Receptor Determinants," <i>The Journal of Immunology</i> , vol. 137, no. 4, 1097-1100 (1986). |
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